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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/547,501	04/12/2000	Samuel T. Christian	IMI-001	6126

7590

02/26/2004

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EXAMINER
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JIANG, SHAOJIA A

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 02/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/547,501

Applicant(s)

CHRISTIAN, SAMUEL T.

Examiner

Shaojia A Jiang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 03 December 2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-42 is/are pending in the application.
- 4a) Of the above claim(s) 1-3, 6-9 and 42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 41, 4-5, and 10-40 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

This Office Action is a response to Applicant's amendment and response filed on December 3, 2003 wherein the instant specification has been amended as to page 3, 37, 51 with respect to incorporate US 6,548,484 (09/547,506) into the instant specification; claims 41, 4-5, and 10-40 have been amended. As recorded in the previous Office Action July 1, 2003, Claims 1-3 and 6-9, 42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Currently, claims 1-42 are pending in this application.

Claims 41, 4-5, and 10-40 as amended now are examined on the merits herein.

Applicant's amendment filed on December 3, 2003 with respect to the rejection of claims 4-5, 11-20 and 23-40 made under 35 U.S.C. 112 second paragraph for the use of the indefinite expressions, of record stated in the Office Action dated July 1, 2003 have been fully considered and found persuasive to remove the rejection. Therefore, the said rejection is withdrawn.

The following is new rejection(s) necessitated by Applicant's amendment filed on December 3, 2003, wherein the limitations in the claims have been changed.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 41, 4-5, and 10-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation, "R<sub>7</sub>" in Formula I in claim 41, is not understood to one of ordinary skill in the art since there is no definition of "R<sub>7</sub>" in Formula I herein. Therefore, the scope of claims is indefinite as to the method encompassed thereby.

The recitation "each of "- in claim 41 is unclear as to what it represents.

Claim 10 recites the limitation "X and Y" in line 7 of the claim "each of X and Y, when present is a carbon atom, a halogen atom or a lower alkyl" and Claim 11 recites the limitation "comprising X and Y comprising a halogen" render these claims indefinite since a halogen atom in the formula herein violates the basic chemical rule.

Claim 11 recites the limitation "comprising X and Y comprising a halogen or oxygen" in line 3 of the claim. There is insufficient antecedent basis for this limitation in the claim since claim 10 does not recited any X and Y being oxygen.

The recitation "selected from TABLE A or from TABLE B " in claims 41 renders the these claims indefinite. Applicant is requested to note that each claim must be self-contained.

It is noted in claim 21 that a period is missing in this claim. According to MPEP 608.01(m) "Each claim begins with a capital letter and ends with a period".

It is noted in claim 23 that the recitation "a sugar is further selected from the group.." is not proper since Applicant is requested to note that a claim which depends

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from a claim, i.e., claim 22, which "consists of" the recited elements or steps cannot add an element or step.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 41, 4-5, and 10-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Likhoshersfov et al. (of record) in view of Mizuma et al. (72 and 73, PTO-1449 submitted November 13, 2000) and Takata et al. (96, PTO-1449 submitted November 13, 2000), and Vannucci et al. (99, PTO-1449 submitted November 13, 2000).

Likhoshersfov et al. discloses the incorporation of carbohydrate residues into active compounds such as dopamine to form dopamine glycoconjugates, the instant elected species (see abstract).

Likhoshersfov et al. does not expressly disclose the employment of the incorporation of carbohydrate residues into active compounds (active drugs) such as dopamine glycoconjugates in a composition and a method for improving the aqueous solubility and blood brain barrier penetrability of a drug.

Mizuma et al. teaches that sugar-conjugated drugs such as glucose-conjugated compounds provide these compounds (drugs) with a new route by the way of the

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glucose transport carrier for better absorption in intestine, improving the poorly absorbable drugs (see abstract).

Both Takata et al. and Vannucci et al. teach the transport of glucose across the blood-tissue barriers such as blood-brain barrier (see abstracts).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ conjugates of carbohydrate residues and active compounds (active drugs) such as dopamine glycoconjugates in a composition and a method for improving the aqueous solubility and blood brain barrier penetrability of a drug.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ conjugates of carbohydrate residues and active compounds (active drugs) such as dopamine glycoconjugates in a composition and a method for improving the aqueous solubility and blood brain barrier penetrability of a drug, since active compounds (active drugs) such as dopamine glycoconjugates are known according to Likhoshersfov et al. Moreover, the teachings of Mizuma et al., Takata et al. and Vannucci et al. have provided the motivation to make conjugates of carbohydrate residues and active drug compounds herein since sugar-conjugated drugs such as glucose-conjugated compounds provide these compounds (drugs) with a new route by the way of the glucose transport carrier for better absorption in intestine and improving the poorly absorbable drugs, and also enhancing the blood brain barrier penetrability of a drug.

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Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Applicant's remarks filed December 3, 2003 the rejection made under 35 U.S.C. 103(a) of record in the previous Office Action rejections July 1, 2003 have been fully considered but are not deemed persuasive as further discussed below.

Applicant argues that "the anomeric structure is not disclosed, e.g. whether the resultant modified disaccharide resides in an energetically stable chair or less stable skew or boat conformation. Biological activity of the resultant compound aglycon (morpholine) or glycon moieties. carbonyl-amide moiety connects the relatively reactive morpholino-nitrogen atom to the glucosyl sugar moiety at the C1 position in the sugar, i.e., eliminating the C1 glucosyl hydroxyl residue." However, the instant claims are not limited to any anomeric structure. Therefore, it is irrelevant whether the reference includes those features or not. Moreover one of ordinary skill in the art would question the *enablement* issue for the instant prodrug compound incorporating with numerous drugs in Table A and B encompassed in the claims, whose structures differ completely or substantially. Further, **biological activities, chemical stability and side effects, and possible toxicity** resulting from the instant resultant compounds would also be in question.

It is noted that only two particular compounds, Compound 1 and 2 are disclosed in working examples of the specification. Thus, the specification fails to provide clear and convincing evidence in sufficient support of the broad use of the prodrug compounds incorporating with numerous drugs in Table A and B encompassed in the

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claims. Therefore, Applicant's Examples of the specification have been fully considered but are not deemed persuasive as to the nonobviousness and/or unexpected results of the claimed invention over the prior art since the evidence in the examples is also not commensurate in scope with the claimed invention and does not demonstrate criticality of a claimed range of the ingredients in the claimed method. See MPEP § 716.02(d). Further, the specification does not provide testing results for biological activities, chemical stability and side effects, and possible toxicity of the instant resultant compounds

Therefore, the evidence presented in specification herein is not seen to be clear and convincing in support the nonobviousness of the instant claimed invention over the prior art.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a). Therefore, said rejection is adhered to.

Applicant is suggested to amend the instant claims by limiting the instant structure in claim 41 to the Formula V of Applicant own patent 6,548,484, i.e., claim 1.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).



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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

S. Anna Jiang, Ph.D.  
Patent Examiner, AU 1617  
February 11, 2004

  
**SREENI PADMANABHAN**  
**SUPERVISORY PATENT EXAMINER**

2/22/04